References

1. Erbay A, Ergonul O, Stoddard GJ, Samore MH. Recurrent catheter-related bloodstream infections: risk factors and outcome. *Int J Infect Dis* 2006;**10**:396—400.
2. Mermel LA, Farr BM, Sherertz RJ, Raad II, O'Grady N, Harris JS, et al. Guidelines for the management of intravascular catheter-related infections. *Clin Infect Dis* 2001;**32**:1249—72.
3. Blot S, Vandewoude K. Early detection of systemic infections. *Acta Clin Belg* 2004;**59**:20—3.
4. Colardyn F. Appropriate and timely empirical antimicrobial treatment of ICU infections—a role for carbapenems. *Acta Clin Belg* 2005;**60**:51—62.
5. Kollef M. Appropriate empirical antibacterial therapy for nosocomial infections: getting it right the first time. *Drugs* 2003;**63**:2157—68.
6. Blot SI, Depuydt P, Annemans L, Benoit D, Hoste E, De Waele JJ, et al. Clinical and economic outcomes in critically ill patients with nosocomial catheter-related bloodstream infections. *Clin Infect Dis* 2005;**41**:1591—8.
7. O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, et al. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. *MMWR Recomm Rep* 2002;**51**:1—29.
8. Berenholtz SM, Pronovost PJ, Lipsett PA, Hobson D, Earsing K, Farley JE, et al. Eliminating catheter-related bloodstream infections in the intensive care unit. *Crit Care Med* 2004;**32**:2014—20.
9. Higuera F, Rosenthal VD, Duarte P, Ruiz J, Franco G, Safdar N. The effect of process control on the incidence of central venous catheter-associated bloodstream infections and mortality in intensive care units in Mexico. *Crit Care Med* 2005;**33**:2022—7.
10. Rosenthal VD, Guzman S, Pezzotto SM, Crnich CJ. Effect of an infection control program using education and performance feedback on rates of intravascular device-associated bloodstream infections in intensive care units in Argentina. *Am J Infect Control* 2003;**31**:405—9.

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Thiazolidinediones could be an effective treatment for HIV-associated progressive multifocal leukoencephalopathy

HIV-associated progressive multi-focal leukoencephalopathy (PML) is a severe neurodegenerative disorder that leads to disability and death from fulminant damage to cerebral white matter. PML is caused by human polyoma JC virus, an almost ubiquitous virus normally kept in check by the immune system.[1] PML had been common prior to the advent of highly active anti-retroviral therapy (HAART), and now some cases are being seen in the context of HAART failure[2] and also immune reconstitution syndrome, where a patient's HAART-restored immune system attacks brain tissue.[3] Currently available treatments such as interferon are often ineffective[4] and new approaches are needed. I propose the hypothesis that thiazolidinediones (TZs) such as pioglitazone and rosiglitazone, currently used for treatment of type II diabetes, could potentially slow the course of PML and under the best of circumstances, induce a complete remission.

Both basic science and clinical data lend support to the above idea. TZs have pleiotropic neuroprotective effects that can be demonstrated in several different animal models of neurodegeneration.[5] Neuroprotective effects are believed to be through anti-inflammatory mechanisms mediated by the peroxisome-activated gamma receptor.[5] TZ stimulation of the peroxisome-activated gamma receptor suppresses a multitude of inflammatory cytokines both in cultured cells and in vivo in animal models.[5—7] Furthermore, pioglitazone has been shown to reduce activation of T lymphocytes from patients with multiple sclerosis,[8] and there is a published case report from 2004 of a 44-year-old woman with severe progressive multiple sclerosis, complicated by quadriparesis, ataxia, fatigue and cognitive decline, who had a significant clinical remission taking pioglitazone.[5] Large scale clinical trials with multiple sclerosis patients are undoubtedly underway now. Given that multiple sclerosis and PML are both demyelinating inflammation of the cerebral white matter, it would be logical to similarly initiate clinical trials in patients with HIV-associated PML. The trials could be either large randomized placebo controlled studies or '*n* of 1' longitudinal studies like that for the patient with multiple sclerosis. TZs already show promise as a treatment for HAART-associated lipodystrophy[9,10] so from an ethical standpoint potential benefits to patients would certainly justify open-label '*n* of 1' studies, if they are done by HIV specialists who would insure no deleterious drug interactions with HAART medications.

In conclusion, potential benefits of TZs for HIV-associated PML warrant further investigation.

Conflict of interest: No conflict of interest to declare.

References

1. Chapagain ML, Nguyen T, Bui T, Verma S, Nerurkar VR. Comparison of real-time PCR and hemagglutination assay for quantitation of human polyomavirus JC. *Virol J* 2006;**3**:3.
2. Langford TD, Letendre SL, Marcotte TD, Ellis RJ, McCutchan JA, Grant I, et al. Severe, demyelinating leukoencephalopathy in AIDS patients on antiretroviral therapy. *AIDS* 2002;**16**: 1019—29.

3. Vendrely A, Bienvenu B, Gasnault J, Thiebault JB, Salmon D, Gray F. Fulminant inflammatory leukoencephalopathy associated with HAART-induced immune restoration in AIDS-related progressive multifocal leukoencephalopathy. *Acta Neuropathol (Berl)* 2005;**109**:449—55.
4. Nath A, Venkataramana A, Reich DS, Cortese I, Major EO. Progression of progressive multifocal leukoencephalopathy despite treatment with beta-interferon. *Neurology* 2006;**66**: 149—50.
5. Pershadsingh HA, Heneka MT, Saini R, Amin NM, Broeske DJ, Feinstein DL. Effect of pioglitazone treatment in a patient with secondary multiple sclerosis. *J Neuroinflammation* 2004;**1**:3.
6. Storer PD, Xu J, Chavis J, Drew PD. Peroxisome proliferator-activated receptor-gamma agonists inhibit the activation of microglia and astrocytes: implications for multiple sclerosis. *J Neuroimmunol* 2005;**161**:113—22.
7. Meier CA, Chicheportiche R, Juge-Aubry CE, Dreyer MG, Dayer JM. Regulation of the interleukin-1 receptor antagonist in THP-1 cells by ligands of the peroxisome proliferator-activated receptor gamma. *Cytokine* 2002;**18**:320—8.
8. Schmidt S, Moric E, Schmidt M, Sastre M, Feinstein DL, Heneka MT. Anti-inflammatory and antiproliferative actions of PPAR-gamma agonists on T lymphocytes derived from MS patients. *J Leukoc Biol* 2004;**75**:478—85.
9. Hadigan C, Yawetz S, Thomas A, Havers F, Sax PE, Grinspoon S. Metabolic effects of rosiglitazone in HIV lipodystrophy: a randomized, controlled trial. *Ann Intern Med* 2004;**140**: 786—94.
10. Calmy A, Hirschel B, Hans D, Karsegard VL, Meier CA. Glitazones in lipodystrophy syndrome induced by highly active antiretroviral therapy. *AIDS* 2003;**17**:770—2.

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A case of human immunodeficiency virus infection disclosed by cytomegalovirus encephalitis

We report herein an unusual case of human immunodeficiency virus (HIV) infection disclosed by hypothalamic amenorrhea and cytomegalovirus (CMV) encephalitis.

One year before admission the patient presented with amenorrhea, mild gait unsteadiness, anorexia, easy fatigability and weight loss (10 kg). Eight months before admission she had visited a gynecologist who prescribed hormonal therapy for amenorrhea, without any effect. Laboratory tests performed at the time showed anemia with increased serum ferritin. At the same time, the patient visited a psychiatrist, who prescribed an antidepressant. Due to the unresponsiveness of the patient's symptoms to the antidepressant treatment, a head CT scan was performed, which was normal. The patient was admitted to the endocrinology department for investigation of amenorrhea.

Hormonal evaluation on admission showed normal serum luteinizing hormone (LH: 2.18 mIU/ml) and follicle-stimulating hormone (FSH: 2.69 mIU/ml) concentrations, and an exaggerated LH (40.93 mIU/ml) and FSH (24.93 mIU/ml) activity after gonadotropin-releasing hormone (GnRH) administration.

The patient was diagnosed as having hypothalamic amenorrhea and hormonal replacement therapy was prescribed. On neurological examination the patient was alert, but had a low score (23/30) on mini-mental status examination (MMSE). She presented involuntary choreiform movements of the upper and lower extremities and was unable to perform the tandem walking test. She presented dysdiadochokinesia and the deep tendon reflexes were symmetrically increased. A magnetic resonance imaging (MRI) examination of the brain was performed and demonstrated diffuse hyperintense areas on T_2-weighted sequences in the periventricular white matter, as well as in the centrum semiovale bilaterally. The abnormal areas were located mainly in the occipital lobes and there was no evidence of mass effect or contrast enhancement (Figure 1); the patient refused any further investigation and she was discharged.

Three months later she was re-admitted to the neurology department due to deteriorating gait unsteadiness. Her MMSE

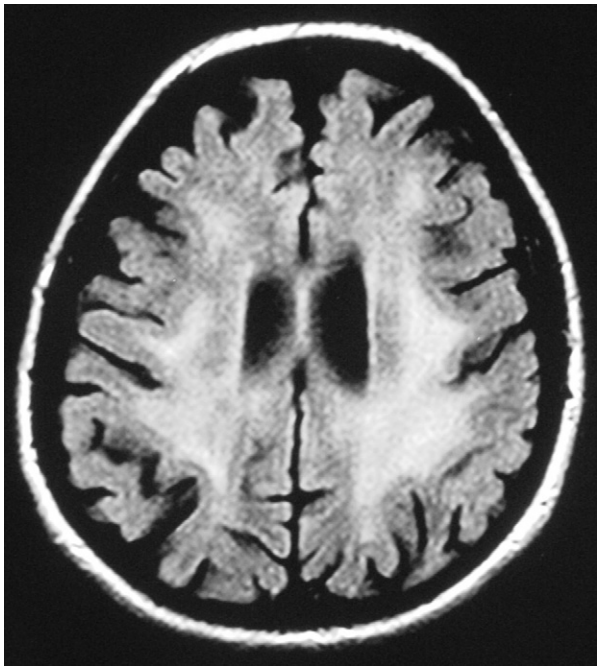

Figure 1 Axial, FLAIR image demonstrates diffuse, ill-defined hyperintense areas in the periventricular white matter, without significant mass effect.